sequences of the same which are known and readily available. As the terms have a well-established meaning in the art and the sequences corresponding to those genes are both known and can be obtained by one of skill in the art, the terms ushA gene and aphA gene are definite.

Concerning 5'-inosinic acid or 5'-guanylic acid, Applicants submit herewith and direct the Examiner's attention to select pages from the Merck Index and the entries corresponding to the same demonstrating that the terms 5'-inosinic acid or 5'-guanylic acid are normally used by one of skill in the art to define a nucleoside 5'-phosphate ester. This is also consistent with the description in the present specification found in the paragraph briding pages 1 and 2.

In view of the foregoing, withdrawal of the rejections under 35 U.S.C. § 112, second paragraph is requested.

The rejection of Claims 4 and 5 under 35 U.S.C. § 102(b) over Laird et al is respectfully traversed.

Laird et al describes "E coli mutants incapable of *de novo* purine biosynthesis and also lacking other periplasmic enzymes with 5'-nucleotidase activity (ushA and aphA)." However, Laird et al do not describe an Escherichia bacteria with the ushA and aphA genes disrupted and which has an ability to produce and accumulate nucleoside 5'-phosphate esters in a medium. Therefore, Laird et al does not anticipate the present claims and as such withdrawal of this ground of rejection is requested.

The rejection of Claims 4 and 5 under 35 U.S.C. § 103(a) over Thaller et al alone or in view of Cowman et al is respectfully traversed.

Thaller et al describe the identification of the aphA gene and on page 197, second paragraph that the aphA gene is a "physiological equivalent to the ushA gene." Thaller et al further describe "characterization of the parameters of this enzyme toward selected substrates, along with investigations on strains carrying genetically defined aphA mutations, are warranted to understand the physiological role of this class of highly conserved bacterial enzymes and to ascertain the significance of the phosphotransferase activities shown by these enzymes under laboratory conditions" (see page 198, col. 1). Therefore, while Thaller et al may describe the potential usefulness of studying aphA by mutating the gene, Thaller et al does not describe the claimed bacterium which has both the ushA and aphA genes disrupted and which has an ability to produce and accumulate nucleoside 5'-phosphate esters in a medium. Cowman et al merely describes the cloning of the ushA gene but also does not describe the nucleoside 5-phosphate ester producing and accumulating property found when the ushA gene and aphA genes have been disrupted in the bacteria. Therefore, in combination, the cited prior art provides no description for the claimed invention.

As shown in Tables 6 and 7 on pages 35 and 37, respectively, disruption of both genes facilitated the production and accumulation of IMP and GMP in the medium. For the Examiner's reference Table 6 is reproduced below:

| Strain | Culture time (h) | Inosine (g/L) | IMP (g/L) |
|---|---|---|---|
| I/pMWpurFKQ | 48<br>48 | 2.3<br>2.3 | 0<br>0 |
| IΔushA/pMWpurFKQ | 51<br>51 | 3.1<br>2.9 | 0<br>0 |
| IΔaphA/pMWpurFKQ | 51<br>51 | 3.6<br>3.2 | 0<br>0 |
| IΔushAΔ/aphA/pMWpurFKQ | 54<br>54 | 2.4<br>2.6 | 1.0<br>0.6 |

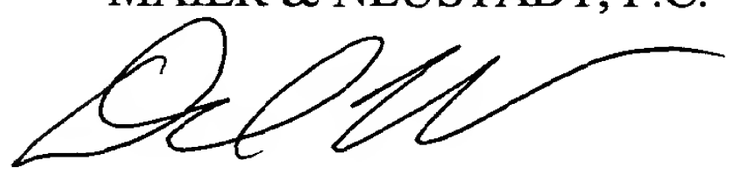
The data in this Table demonstrate that only the bacterial strain deficient in both genes (row 4) was able to produce and accumulate IMP and the medium compared to either gene mutant alone (rows 2 and 3) or the parental strain (row 1). Therefore, even if one assumes that it would have been obvious to disrupt both genes, there would not have been an expectation that disrupting both genes rather than each individually would facilitate the production of nucleoside 5'-phosphate esters. This is particularly so in light Thaller et al who describes the aphA gene is a physiological equivalent of ushA gene

Therefore, the present claims are not obvious in view of the combination of Thaller et al and Cowman et al. Withdrawal of this ground of rejection is requested.

Applicants submit the present application is ready for allowance. Early notification of such allowance is kindly requested.

Respectfully submitted,

OBLON, SPIVAK, McCLELLAND,
MAIER & NEUSTADT, P.C.



Norman F. Oblon
Attorney of Record
Registration No. 24,618

Daniel J. Pereira, Ph.D.
Registration No. 45,518

22850

(703) 413-3000
Fax #: (703) 413-2220

IN THE CLAIMS

4. (Amended) [A] An isolated bacterium belonging to the genus Escherichia having an ability to produce and accumulate nucleoside 5'-phosphate ester in a medium, in which ushA gene and aphA gene are disrupted.

5. (Amended) The isolated bacterium belonging to the genus Escherichia according to Claim 4, wherein the nucleoside 5'-phosphate ester is selected from the group consisting of 5'-inosinic acid or 5'-guanylic acid.

Claims 1-3 and 6-8 are canceled.

Claims 9 and 10 are added.

# THE MERCK INDEX

AN ENCYCLOPEDIA OF
CHEMICALS, DRUGS, AND BIOLOGICALS

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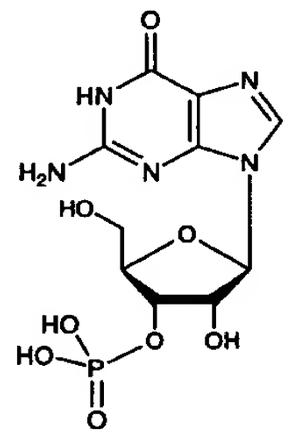
$C_{10}H_{14}N_5O_8P$; mol wt 363.22. C 33.07%, H 3.88%, N 19.28%, O 35.24%, P 8.53%. From yeast or pancreas. Prepn: P. A. Levene, L. W. Bass, *Nucleic Acids* (New York, 1931) pp 224-227. Structure: Levene, Jorpes, *J. Biol. Chem.* **81,** 579 (1929); Levene, Harris, *ibid.* **95,** 755 (1932); **98,** 9 (1932). Early work probably done on a mixture of 2′- and 3′-guanylic acids; see physical data below. Separation of two isomers: Cohn, *J. Am. Chem. Soc.* **72,** 1471 (1950); Khym, Cohn, *ibid.* **76,** 1818 (1954); *eidem, Biol. Prepn.* **5,** 40 (1957). Absorption spectrum: Voet *et al., Biopolymers* **1,** 193 (1963). *Reviews: see* Guanine, Nucleic Acids.

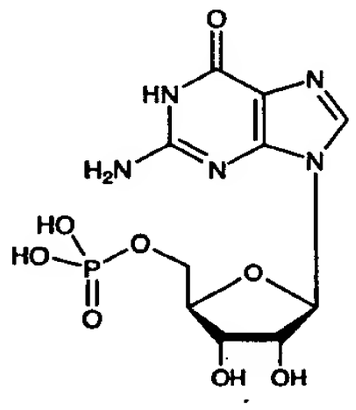


Dihydrate, long prisms from water. The water of crystn is given up at 118° and is taken up again at room temp. When anhydrous, dec 180° (closed tube). $[\alpha]_D^{25}$ −8° (c = 2); −65° (c = 2 in 5% NaOH). Acid to litmus. Soluble in cold water, freely sol in hot water. Boiling with dil mineral acids yields guanine, $H_3PO_4$, and D-ribose.

Neutral sodium salt, $Na_2C_{10}H_{12}N_5O_8P$, flakes from water, contains 21.1% $H_2O$. Sol in cold, freely sol in hot water.

Brucine salt heptahydrate, $C_{10}H_{14}N_5O_8P.(C_{23}H_{26}N_2O_4)_2.7H_2O$, rectangular leaflets from alc. When anhydr, dec 233-240°. $[\alpha]_D^{20}$ −26° (35% alc). One gram dissolves in 100 ml water.

**4600. 5′-Guanylic Acid.** Guanosine 5′-monophosphate; GMP; guanosine 5′-phosphate; guanine riboside-5-phosphoric acid. $C_{10}H_{14}N_5O_8P$; mol wt 363.22. C 33.07%, H 3.88%, N 19.28%, O 35.24%, P 8.53%. Nucleotide widely distributed in nature; found in hydrolyzates of RNA. Isolated together with inosinic acid from sardines or yeast extract: Kuninaka *et al., New Food Ind. (Tokyo)* **3,** no. 1, 21 (1961). Also by direct biosynthesis using microorganisms or enzymes: Abrams, Bentley, *Arch. Biochem. Biophys.* **79,** 91 (1959); Magasanik, Karibian, *J. Biol. Chem.* **235,** 2672 (1960); Okumura *et al.,* U.S. pat. **3,249,511** (1966). Chemical synthesis: Michelson, Todd, *J. Chem. Soc.* **1949,** 2483; Chambers *et al., J. Am. Chem. Soc.* **79,** 3747 (1957); Gilham, Tener, *Chem. & Ind. (London)* **1959,** 542; Tener, *J. Am. Chem. Soc.* **83,** 159 (1961); Koransky *et al., Z. Naturforsch.* **17B,** 291 (1962). Prepn of Na salt: Ishibashi, Ito, U.S. pat. **3,190,877** (1965 to Takeda). Monograph on synthesis of nucleotides: G. R. Pettit, *Synthetic Nucleotides* **vol. 1** (Van Nostrand Reinhold, New York, 1972) 252 pp. *Reviews: See* Guanidine; Nucleic Acids.



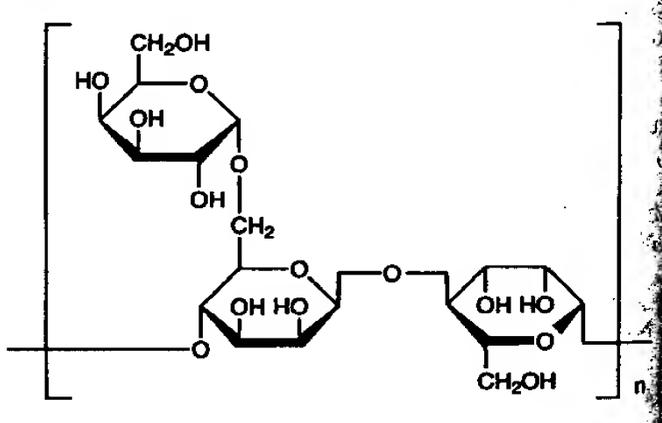
Microcrystals, dec 190-200°. Sparingly sol in cold water.

Barium salt octahydrate, $C_{10}H_{12}N_5O_8PBa.8H_2O$, white powder. uv max (pH 2): 256 nm (ε 12400); (pH 12): 260 nm (ε 12100).

Disodium salt monohydrate, $C_{10}H_{12}N_5O_8PNa_2.H_2O$, [illegible] groscopic crystals, decomp at about 250°. Charact[illegible] meaty taste. $a_M$ (molar absorbancy): 13.7 × $10^3$ at [illegible] nm (pH 7). Soly in water at 25° about 25 g/100 ml. P[illegible] tically insol in alcohol, acetone, ether.

USE: The disodium salt as flavor intensifier, like so[illegible] inosinate and sodium glutamate. Said to be more effe[illegible] than either.

**4601. Guaran.** Principal polysaccharide from [illegible] sperm of guar seeds, *Cyamopsis tetragonaloba* (L.) T[illegible] *Leguminosae:* Heyne, Whistler, *J. Am. Chem. Soc.* 70, [illegible] (1948). Structure: Whistler, Durso, *ibid.* **74,** 5140 ([illegible] Configuration: Koleske, Kurath, *J. Polymer Sci.* Pt [illegible] 4123 (1964). *Review:* Deuel *et al., Chimia* **8,** 64 (195[illegible]



$[\alpha]_D^{25}$ +53° (1*N* NaOH). Sol in cold water.

Triacetate, fibrous material, mp 226-227°. Can be [illegible] into strong films which can be elongated 550%. Bec[illegible] birefringent and does not develop crystallinity.

USE: In textile and paper industry.

**4602. Guar Gum.** Guar flour; gum cyamopsis; [illegible] mopsis gum; Burtonite V-7-E; Jaguar; Decorpa; Gu[illegible] Glucotard; Guarem. Mol wt about 220,000. The gr[illegible] endosperms of *Cyamopsis tetragonolobus* (L.) Taub[illegible] *minosae* which is cultivated in India as livestock feed[illegible] water soluble fraction (85%) of guar flour is called g[illegible] which consists of linear chains of (1→4)-β-D-manno[illegible] nosyl units with α-D-galactopyranosyl units attache[illegible] (1→6) linkages. Ratio of D-galactose to D-mannose [illegible] Effect on lipid metabolism: D. J. A. Jenkins *et al.,* [illegible] *Med. J.* **2,** 1555 (1979); on glucose and lipid levels i[illegible] betic and healthy volunteers: U. Smith, G. Holm, A[illegible] *sclerosis* (Shannon, Ire.) **45,** 1 (1982); on renal tume[illegible] diabetic rats: B. C. Chin *et al., Biomed. Res.* **5,** 27[illegible] As source of fiber in patients with non-insulin dep[illegible] diabetes: M. E. McIvor *et al., Am. J. Clin. Nutr.* [illegible] (1985). Toxicology studies: S. L. Graham *et al., Food* [illegible] *met. Toxicol.* **19,** 287 (1981). Comprehensive mono[illegible] F. Smith, R. Montgomery, *The Chemistry of Plant* [illegible] *and Mucilages* (Reinhold, New York, 1959) 627 pp. [illegible] Goldstein *et al.* in *Industrial Gums,* R. L. Whistl[illegible] (Academic Press, New York, 2nd ed., 1973) p 303 ff

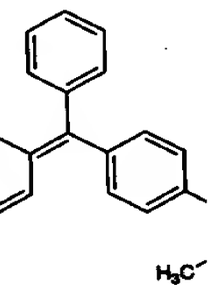
Free flowing powder. Completely sol in cold [illegible] water; practically insol in oils, greases, hydrocarbo[illegible] tones, esters. Water solns are tasteless, odorless, n[illegible] of a pale, translucent gray color, and neutral. S[illegible] heat. Has five to eight times the thickening power of [illegible] Water solns may be converted to a gel by small amo[illegible] borax. Aq dispersions are neutral. *Cf.* "A Com[illegible] Study of Commercially Available Guar Gums" by [illegible] Schlakman, A. J. Bartilucci, *Drug Standards* **25,** [illegible] (1957). $LD_{50}$ in male, female rats (g/kg): 7.35, 6.7[illegible] (Graham).

USE: In paper sizing; as a protective colloid, s[illegible] thickening and film forming agent for cheese, sala[illegible] ings, ice cream, soups; as a binding and disintegrati[illegible] in tablet formulations; in pharmaceutical jelly formu[illegible] in suspensions, emulsions, lotions, creams, toothp[illegible] the mining industry as a flocculant, as a filtering a[illegible] water treatment as a coagulant aid.

THERAP CAT: Adjunct to diet, insulin or oral [illegible] cemics in control of diabetes.

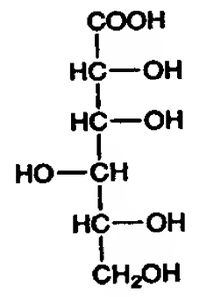
**4603. Guinea Green B.** *N-Ethyl-N-[4-[[4-[ethyl[illegible] fophenyl)methyl]amino]phenyl]phenylmethylene]*[illegible]

*dien-1-ylidene]-3-sulfobenzeneme[illegible] sodium salt;* C.I. Acid Green 3; C.[illegible] Green 1; C.I. 42085. $C_{37}H_{35}N_2Na$[illegible] 4.33%, H 5.11%, N 4.06%, Na [illegible] Prepn: Jones *et al., J. Assoc.* [illegible] (1955). Toxicity studies: F. C. [illegible] *J.* **97,** 30 (1964); W. H. Hanse[illegible] *col.* **4,** 389 (1966). *See also: Col[illegible]* 1971) p 4385.



dull, dark green powder, or a bi[illegible] water to a green soln which bec[illegible] dd[illegible] of HCl and blackish-green w[illegible] OH decolorizes the soln. Spari[illegible] es in concd $H_2SO_4$ to a yellow [illegible] with water, turns first yellowish-[illegible] in rats: >2 g/kg (Lu, Lavalle[illegible] Limited use as a dye for silk [illegible] gical stain. Delisted by FDA in [illegible] and cosmetics.

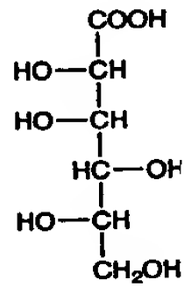
**D-Gulonic Acid.** $C_6H_{12}O$[illegible] %, H 6.17%, O 57.09%. Prepd [illegible] ion of sodium glucuronate wit[illegible] ne medium: Fischer, Piloty, *Be*[illegible] onic acid γ-lactone: Rehorst, [illegible]



[illegible] 6° (10 min) → −38.6° (1[illegible] ic lactone spontaneously. p[illegible] um salt, $C_6H_{11}NaO_7$, crystals

um salt, $Ca(C_6H_{11}O_7)_2$. $[\alpha]_D$[illegible] ated from aq soln by alc.

**L-Gulonic Acid.** Xylose[illegible] wt 196.16. C 36.74%, H 6 [illegible] ylose and HCN followed [illegible] scher, Stahel, *Ber.* **24,** 529 [illegible] ic acid: Ger. pat. **618,907** [illegible] from L-gulonolactone: [illegible] *Bull.* **13,** 173 (1965).

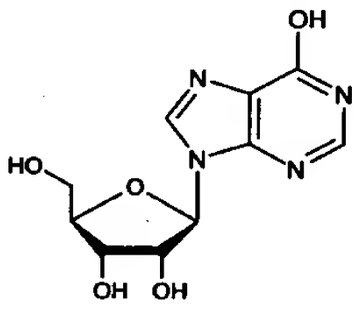


[illegible] izes as the lactone on eva[illegible] um salt, $[\alpha]_D^{20}$ +12.7° (c = 9[illegible]

**D-Gulose.** $C_6H_{12}O_6$; mc[illegible] O 53.28%. Prepd by so[illegible] al soln of the γ-lactone of

1986) pp 408-418. *Reviews:* F. H. de Jong, *Oxford Rev. Reprod. Biol.* **9**, 1-53 (1987); N. Ling *et al., Vitam. Horm.* (New York) **44**, 1-46 (1988).

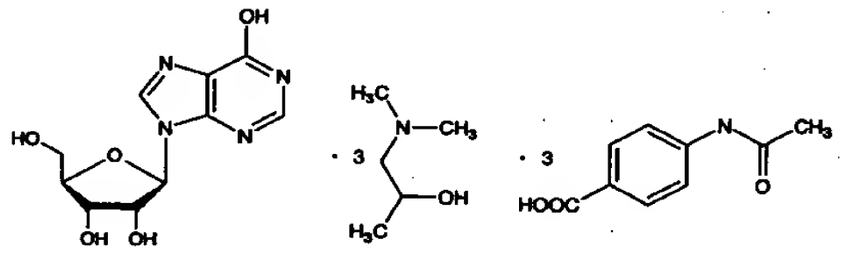
**5005. Inosine.** Hypoxanthine riboside; 9-β-D-ribofuranosylhypoxanthine; hypoxanthosine; Inosie; Oxiamine; Ribonosine; Trophicardyl. $C_{10}H_{12}N_4O_5$; mol wt 268.23. C 44.78%, H 4.51%, N 20.89%, O 29.82%. In meat and meat extracts, in sugar beets. Prepd from adenosine by incubation with purified adenosine deaminase from intestine: Kalckar, *J. Biol. Chem.* **167**, 445 (1947); also by the action of sodium nitrite and acetic acid on adenosine: Levene, Jacobs, *Ber.* **43**, 3161 (1910); by the use of barium nitrite and $H_2SO_4$: Reiff *et al.*, U.S. pat. **3,049,536** (1962 to Zellstoff-Fabrik Waldhof). Fermentation method: Motozaki *et al.*, U.S. pat. **3,111,459** (1963 to Ajinomoto). Structure: Bredereck, *Ber.* **66**, 198 (1933); *Z. Physiol. Chem.* **223**, 61 (1934); Gulland, Holiday, *J. Chem. Soc.* **1936**, 765.



Dihydrate, long rectangular plates from water, mp 90°. Anhydrous needles from 80% alc, dec 218° (rapid heating). $[\alpha]_D^{18}$ −49.2° (c = 0.9 in $H_2O$). $[\alpha]_{white}^{20}$ −73° (0.5 g + 2 ml *N* NaOH + 3 ml $H_2O$). 100 ml of the satd water soln at 20° contain 1.6 g inosine. Absorption spectrum: Kalckar, *loc. cit.* uv max (pH 6.0): 248.5 nm (ε 12200). Boiling with 0.1*N* $H_2SO_4$ yields hypoxanthin and D-ribose.

THERAP CAT: Activates cellular functions.

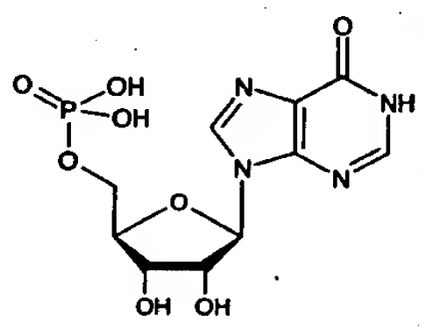
**5006. Inosine Pranobex.** ***Inosine mono[4-(acetylamino)benzoate] (salt) compd with 1-(dimethylamino)-2-propanol (1:3);*** inosine:dimethylaminoisopropanol acetamidobenzoate (1:3); inosiplex; methisoprinol; NP-113; NPT-10381; Aviral; Delimmun; Imunoviral; Isoprinosin; Isoprinosina; Isoprinosine; Isoviral; Modimmunal; Pranosina; Pranosine; Viruxan. $C_{52}H_{78}N_{10}O_{17}$; mol wt 1115.25. C 56.00%, H 7.05%, N 12.56%, O 24.39%. Immunostimulant complex formed from the *p*-acetamidobenzoate salt of dimethylaminoisopropanol and inosine in a 3:1 molar ratio. Prepn: P. Gordon, Ger. pat. **1,965,431**; *idem*, U.S. pat. **3,646,007** (1971, 1972 both to Newport Pharm.). Antiviral activity: E. R. Brown, P. Gordon, *Can. J. Microbiol.* **18**, 1463 (1972); R. L. Muldoon *et al., Antimicrob. Ag. Chemother.* **2**, 224 (1972). Stimulatory effect on T-cell function: L. Binderup, *Int. J. Immunopharmacol.* **7**, 93 (1985). Pharmacology and therapeutic potential: D. M. Campoli-Richards *et al., Drugs* **32**, 383 (1986). Clinical immunopharmacology: A. J. Glasky, J. F. Gordon, *Cancer Detect. Prev. Suppl.* **1**, 597 (1987). Clinical trial in subacute sclerosing panencephalitis (SSPE): C. E. Jones *et al., Lancet* **1**, 1034 (1982); G. Gascon *et al., Brain Devel.* **15**, 346 (1993). Clinical trial in pre-AIDS patients: C. Pedersen *et al., N. Engl. J. Med.* **322**, 1757 (1990). Review of efficacy in HIV infection: C. De Simone *et al., Int. J. Immunopharmacol.* **13**, Suppl. 1, 19-27 (1991).



Neutral water-soluble solid. $LD_{50}$ in mice and rats (mg/kg): >4000 orally and i.p. (Gordon).

THERAP CAT: Immunomodulator; antiviral.

**5007. Inosinic Acid.** ***5′-Inosinic acid;*** 5-inosinic acid; muscle inosinic acid; t-inosinic acid; hypoxanthine riboside-5-phosphoric acid; IMP. $C_{10}H_{13}N_4O_8P$; mol wt 348.2[illegible] 34.49%, H 3.76%, N 16.09%, O 36.76%, P 8.90%. [illegible] from meat extract: Levene, Bass, *Nucleic Acids* (New Y[illegible] 1931) p 229; from dried sardines: Yoshida, Kagey[illegible] **Japan.** pat. **732('56)** (to Ajinomoto), *C.A.* **51**, 3870b[illegible] Structure: Levene, Bass, *op. cit.*, pp 187-192; Breder[illegible] *Ber.* **66**, 198 (1933); Levene, Tipson, *J. Biol. Chem.* **111**[illegible] (1935). Also prepd from muscle by enzymatic deam[illegible] tion of muscle adenylic acid: Ostern, *Biochem. Z.* **254**[illegible] (1932); by hydrolysis of inosine triphosphate: Kleinz[illegible] *Biochem. J.* **36**, 729 (1942). Studies on the enzymatic [illegible] thesis: Greenberg, *J. Biol. Chem.* **190**, 611 (1951); Kor[illegible] *al., ibid.* **217**, 875 (1955). Microbial fermentation me[illegible] using mutant strains of *Micrococcus glutamicus:* Kinos[illegible] *et al.*, U.S. pat. **3,232,844** (1966 to Kyowa).



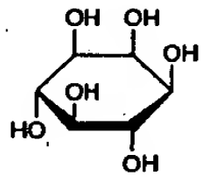
Syrup, solidifies to a glass when dried over $H_2S$[illegible] Agreeable sour taste. $pK_1$ = 2.4; $pK_2$ = 6.4. Absorp[illegible] spectrum: Kalckar, *J. Biol. Chem.* **167**, 445 (1947). Fr[illegible] sol in water, in formic acid; very sparingly sol in alco[illegible] ether. On boiling with acid hydrolyzes to 1 mol $H_3PO_4$[illegible] mol hypoxanthine, 1 mol D-ribose.

Disodium salt dihydrate, $C_{10}H_{11}N_4Na_2O_8P.2H_2O$, [illegible] sol in alcohol, ether, acetone; soly in water at 20° abou[illegible] g/100 ml. Kawasaki, *New Food Ind. (Tokyo)* **3**, no. [illegible] (1961).

Barium salt, $C_{10}H_{11}BaN_4O_8P$. Hemipentadecahydr[illegible] lustrous leaflets. Becomes anhydr at 100° *in vacuo*. [illegible] −18.5° (0.3 g of anhydr Ba salt in 10 ml of 2.5% HCl)

USE: Its salts as flavor intensifiers, like sodium glutam[illegible] Examples of mixtures of sodium inosinate and sodium [illegible] tamate or other salts: Toi *et al.*, U.S. pat. **3,109,741** [illegible] to Ajinomoto).

**5008. Inositol.** ***myo-Inositol;*** *meso*-inositol; *i*-inos[illegible] hexahydroxycyclohexane; cyclohexanehexol; cyclohe[illegible] meat sugar; inosite; mesoinosite; phaseomannite; dam[illegible] nucite; bios I; rat antispectacled eye factor; mouse ant[illegible] pecia factor. $C_6H_{12}O_6$; mol wt 180.16. C 40.00%, H 6.[illegible] O 53.28%. Widely distributed in plants and anim[illegible] Growth factor for animals and microorganisms. Isoln [illegible] heart muscle: Scherer, *Ann.* **73**, 322 (1850); from [illegible] Woolley, *J. Biol. Chem.* **139**, 29 (1941). Synthesis: [illegible] land, Wishart, *Ber.* **47**, 2082 (1914); Anderson, Walt[illegible] *Am. Chem. Soc.* **70**, 2931 (1948). Obtained commer[illegible] from corn steep liquor, since inositol is present as ph[illegible] acid in corn: Bartow, Walker, *Ind. Eng. Chem.* **30**[illegible] (1938); U.S. pat. **2,112,553** (1938); Hoglan, Bartow, *J.* [illegible] *Chem. Soc.* **62**, 2397 (1940); Elkin, Meadows, U.S. [illegible] **2,414,365** (1947); Brit. pat. **601,273** (1948 to Corn [illegible] Refining). Nine possible stereoisomers: Seven are opti[illegible] inactive or *meso*. Two optically active forms, the ra[illegible] form, and several *cis,trans*-isomers occur naturally. Di[illegible] valent natural form is *cis*-1,2,3,5-*trans*-4,6-cyclohexane[illegible] which is described here. *Reviews:* R. Beckmann, *Zu*[illegible] (Editio Cantor, Aulendorf, 1953); several authors in *Vitamins,* **vol. 2**, W. H. Sebrell, Jr., R. S. Harris, Eds. [illegible] demic Press, New York, 1954) pp 321-386; *ibid.* vol. [illegible] ed., 1971) pp 340-415.



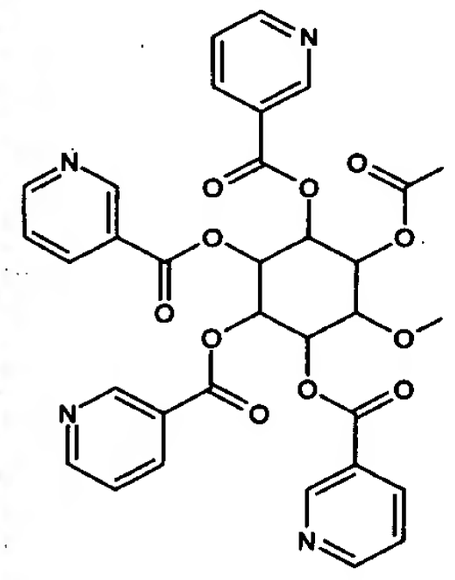
Anhydr, non-hygroscopic crystals from water or [illegible] acid above 80°. Sweet taste. d 1.752. mp 225-227[illegible]

[illegible] inactive. Soly in water at 25°: [illegible] 28 g/100 ml soln. Slightly sol in [illegible] ter and other common organic sol[illegible] [illegible] to litmus.

[illegible] ydrate, efflorescent crystals from [illegible] mp 218°. Becomes anhydr at 1[illegible] [illegible] ophosphate, $C_6H_{13}O_9P$. Prepn: [illegible] *Helv. Chim. Acta* **12**, 1165 (1929); [illegible] *em. Prepn.* **2**, 65 (1952). Crystals [illegible] dec 195-197°. Titrates as a dibasic [illegible] ter (1 g dissolves in 3 ml $H_2O$). P[illegible] [illegible] ol, ether. Remarkably resistant t[illegible] [illegible] ith strong alkali. May be hydrol[illegible] [illegible] Cl for 14 hrs.

[illegible] ERAP CAT: Vitamin B complex; lip[illegible]

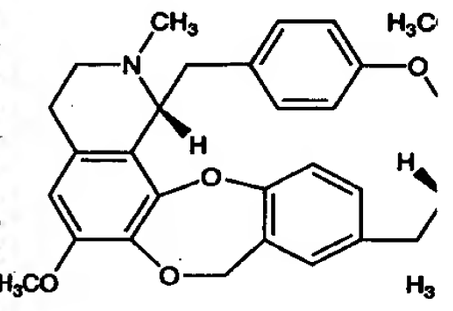
[illegible] 009. **Inositol Niacinate.** ***myo-Ino*** [illegible] *rylate;* hexanicotinoyl inositol; he[illegible] [illegible] ns-4,6-cyclohexane; inositol hexani[illegible] [illegible] exanicotinate; Dilcit; Dilexpal; [illegible] oyannid; Hexanicit; Hexopal; Lin[illegible] [illegible] $C_{42}H_{30}N_6O_{12}$; mol wt 810.73. C [illegible] [illegible] %, O 23.68%. Prepn: Badgett, [illegible] *Soc.* **69**, 2907 (1947).



[illegible] ystals, mp 254.3-254.9°. Practicall[illegible] [illegible] l acids.

[illegible] ERAP CAT: Vasodilator (peripheral)

[illegible] 010. **Insularine.** $C_{38}H_{40}N_2O_6$; [illegible] [illegible] %, H 6.50%, N 4.51%, O 15.46% [illegible] *elos insularis* Makino and *C. oc*[illegible] [illegible] *spermaceae.* Isoln: Kondo, Yanc[illegible] [illegible] 7, 815 (1927); Kondo, Tomita, *A*[illegible] [illegible] 0). Structure: Tomita, Kikuchi, [illegible] [illegible] 7 (1957).



[illegible] orphous powder, $[\alpha]_D^7$ +28°, mp [illegible] Absorption spectrum: Ochai, [illegible] [illegible] 5 (1929).

[illegible] 011. **Insulin.** Polypeptide hormo[illegible] [illegible] beta cells that regulates carbol[illegible] [illegible] ted by proteolysis from the sin[illegible] [illegible] the active dimer composed of [illegible] [illegible] ol wt ~6000. Regulates car[illegible] [illegible] olism, and influences protein syn[illegible] [illegible] protein for which the chemica[illegible] [illegible] determined. Also the first co[illegible] [illegible] produced by recombinant